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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/864,451	05/25/2001	Louis D. Falo JR.	076333-0267	3388

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/864,451	FALO ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 37-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 37-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-12, and newly added Claims 37-40, are pending and being acted upon.

2. Applicant's amendment and response, and the 1.132 declaration of Inventor Falo, filed 7/19/04, are acknowledged.

3. It is noted that a wrong Peters reference was included with the action. Accordingly, the previous rejection under 35 U.S.C. 102(b) has been withdrawn and a new rejection under 35 U.S.C. 102(b) has been made, thus, the instant action has not been made final.

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because, uninitialed changes in the residence address of Inventor Falo have been made.

Applicant argues, "The Office has identified no authority for the proposition that such changes must be initialed."

Applicant is advised that a proper oath or declaration is required. Declarations comprising uninitialed changes are not considered proper. Applicant is further advised that failure provide a properly executed declaration in response to this action will be considered non-responsive.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-12 and newly added Claims 37-40 stand/are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the claimed formulations would comprise effective formulations for prophylactic and therapeutic anti-tumor and

anti-viral immunization, for the reasons of record set forth in the action mailed 2/19/04.

Applicant's arguments, filed 7/19/04, have been fully considered but they are not persuasive. Applicant argues, "In essence, therefore, the Office has asserted non-enablement based on inoperability or lack of utility...The Office has conceded that "Examples 5 and 6 demonstrate efficacy of the invention in an animal model." Office Action, page 3, second paragraph. That should end the inquiry. The Federal Circuit has rejected, as a general proposition, the argument that *in vivo* tests in animals are not predictive of anti-cancer efficacy." Applicant cites *in re Brana* and *in re Krimmel*.

Applicant is advised that no lack of utility rejection has been made. It is the Examiner's position that the specification fails to disclose how to use the composition of the instant claims for its intended use. It is clear that the hybrid cells of the instant claims are not intended to be used as veterinary treatments for induced tumors in mice. Such an intended use would require a utility rejection. The specification refers to the use of the claimed compositions in "patients" and lists a number of diseases/viruses that are either exclusive to humans, e.g., human immunodeficiency virus and human papilloma virus, or treated only in humans, e.g., melanoma, lung carcinoma, prostate carcinoma. Accordingly, it is the Examiner's position that the "patients" of the specification are most probably humans and multiple references have been made of record to show why the administration of the hybrids of the instant claims would not likely provide an effective treatment for cancers or viral infections in humans.

Applicant argues, "The evidence and explanation of record do not show that Bodey et al., Frank et al. and Cohen reflect the existing state of the art when this application was filed. These references were published after the priority date of this application. The state of the art, however, does include numerous patents, granted by the Office before the filing date of this application, with claims drawn to vaccines against cancer and HIV. These patents demonstrate that the nature of the claimed formulations "does not suggest an inherently unbelievable undertaking or involve implausible scientific principles."

Applicant's argument appears to be base on a logic that the claimed formulations might have provided an effective treatment in 1997, but not in 2000 or 2002. Such an argument is not

convincing. Regarding other allowed patents, each application is examined on its own merits by the Examiner of record and no comment on the validity of other U.S. patents will be offered here.

Applicant argues, "Current research dispels any doubt that the Bodey, Frank, and Cohen publications might cast on the utility of the claimed formulations. For example, the results of a recent phase I clinical trial have demonstrated that a dendritic-cell vaccine for renal cancer is safe and effective in boosting cancer patients' immune systems. See Duke University news release of May 1, 2003 (copy enclosed). Also, a dendritic cell vaccine for simian immunodeficiency virus (SIV) has been recently shown to elicit effective and desirable SIV-specific cellular and humoral immunity. See Wu et al., *Nat. Med.* 9: 27-32, 2003 (copy enclosed)."

This line of argument seems curious in light of the previous argument that references from 2000 and 2002 cannot show a lack of enablement because of the 1997 priority date. It appears then that Applicant is arguing that the formulations of the instant claims were enabled in 1997, it is irrelevant whether or not they were enabled in 2000 or 2002, and they were again enabled in 2003. This argument is not found to be convincing. Also note that no attachments were received with the instant amendment. Regardless, a news release concerning a phase 1 trial could not enable the formulations of the instant claims because phase 1 trials do not address efficacy. Phase 1 trials primarily address safety with secondary consideration given to bioavailability, pharacokinetics, and dosing regimens/ranges. Regarding the formulation and model of Wu et al., neither the formulation (an antigen pulsed DC) nor the model (SIV) are those of the instant claims and application. Further, while some formulations have shown some efficacy in SIV models, no corresponding formulations have as yet demonstrated efficacy versus HIV.

As Applicant has indicated that more recent findings and conclusions should be given more thorough consideration, it is noted that Roberts, 2004, in a publication entitled, *Are HIV Vaccines Fighting Fire with Gasoline?*, teaches that activating T cells in an attempt to fight HIV may actually exacerbate disease. The reference notes that HIV preferentially infects, and grows better in, activated T cells. As activated T cells are the intended result of the administration of the hybrid APCs of the instant claims, it appears that the most recent of publications still casts doubt upon the efficacy of the use of the claimed

invention. Clearly, the use of the claimed formulations is at best highly unpredictable even now and, thus, highly unpredictable as of the 1997 priority date.

Applicant concludes by asserting that the claimed invention could be used without undue experimentation, "To carry out the claimed invention, a person of skill in the art would need to know (1) how to prepare the claimed formulation comprising a macrophage or dendritic cell fused to a tumor cell or a virally infected cell and (2) how to administer the formulation to a patient."

It remains the Examiner's position that the "how to use" provision additionally requires that the administration of the formulation of the instant claims provide some efficacy. Said efficacy has not been adequately established.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-3, 5-8, 10-12, and newly added Claims 37 and 39, stand/are rejected under 35 U.S.C. 102(a) as being clearly anticipated by WO 96/30030, for the reasons of record set forth in the action mailed 2/19/04.

Applicant's arguments, filed 7/19/04, have been fully considered but they are not persuasive. Applicant argues that the newly submitted 1.132 declaration of Inventor Falo antedates the reference.

Applicant is advised that the new declaration does not disclose the entire invention of the instant claims and, thus, fails to show that Applicant was in possession of the invention as claimed before 03 October 1996.

The declaration teaches only a mouse DC fused with a tumor cell, specifically a mouse DC fused with a mouse B16 melanoma cell or a DC fused with a 3LL Lewis lung carcinoma cell. The declaration does not teach the claimed generic DC tumor hybrid of

any species nor a hybrid comprising the tumor cell types of Claim 3. Additionally, the reference does not teach a hybrid comprising a macrophage nor a hybrid comprising a virally infected cell. Neither does the declaration teach a hybridoma comprising the first/second cell ratios of Claims 5, 6, 10, or 11.

9. The following is a new ground of rejection.

10. Claims 1-3, 5-6, and newly added Claims 37 and 39, are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Peters (1981).

Peters teaches a formulation comprising a hybridoma having a first DC fused to a sarcoma cell (see entire document). Note that the source of the DC cell is irrelevant to a product claim absent a showing that said source *is* relevant. Further note that while the reference does not indicate the ratio of DCs to tumor cells in the formulation, if the ration did not fall within the 2 to 4 log range of the claims, it is highly unlikely that the author would have been able to purify and analyze the properties of the product.

The reference clearly anticipates the claimed invention.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

13. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

9/20/04

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